

Carrageenan

Brand Name: Carraguard

Drug Class: Microbicides

Drug Description

Carrageenan is a water-soluble mixture of sulfated polysaccharides extracted from red seaweed (Rhodophyceae), or Irish moss, found off the Atlantic coasts. [1] [2] The kappa, iota, and lambda forms of carrageenan are distinguished by the position of sulfate and the presence or absence of anhydrogalactose on the main polysaccharide backbone. Carrageenan, also known as PC-515, is a mixture of lambda and kappa carrageenan. [3] Kappa carrageenans have a helical tertiary structure that allows gelling; lambda carrageenans are non-gelling. [4]

HIV/AIDS-Related Uses

Carrageenan is being investigated in Phase II/III trials as a topical microbicide to prevent the sexual transmission of HIV. A combined kappa and lambda carrageenan formulation comprises the active pharmaceutical ingredient in Carraguard, a vaginal gel being investigated in clinical trials. [5] [6] [7]

Non-HIV/AIDS-Related Uses

Carrageenan is used as a gelling, emulsifying, and stabilizing agent and viscosity builder in foods and nonfoods, particularly in milk and water systems. [8] Carrageenan is used as a clarifier for beverages and is used to suspend cocoa in chocolate manufacturing. [9] Carrageenan is used in cough and cold preparations, topical creams, and medicated shampoos. [10] Carrageenan compounds are on the FDA's list of GRAS (generally recognized as safe) products for consumption and topical application. [11]

Carrageenan is a potent in vitro inhibitor of herpes simplex virus, human cytomegalovirus, vesicular stomatitis virus, and Sindbis virus, in addition to HIV. [12] Laboratory tests have shown that carrageenan gel also blocks human papillomavirus and gonorrhea infection in vitro and in vivo. [13]

Pharmacology

HIV infected macrophages may mediate sexual

transmission of HIV. Carrageenan provides microbicidal activity by blocking macrophage migration, or cell trafficking, from vaginal tissue to lymph nodes. [14] [15] In one study, carrageenan reduced the number of macrophages in lymph nodes by greater than 90% compared to a 50% reduction by placebo. [16] Carrageenan appears to prevent cell trafficking by coating the surfaces of vaginal cells to prevent adhesion of macrophages to the epithelial surface. [17]

Carrageenan is bound to the vaginal epithelium for up to 4 hours. An in vivo study showed that significant quantities of carrageenan could be detected up to 24 hours post-application, and that the duration of activity was retained without loss for three hours. [18]

Carrageenan gel studied in cervical samples did not appear to interfere with testing for other sexually transmitted diseases. [19]

Adverse Events/Toxicity

Phase II safety trials have been conducted in women, who applied carrageenan before each act of intercourse or at least three times weekly. Few adverse effects, including mild itching, burning, and pain, were reported. [20] No women developed visible cervical or vaginal abnormalities. [21] Most women considered the applicator and the gel itself easy to use, not messy, and of reasonable volume. [22] [23] No significant differences in rate of side effects or development of lesions were noted between gel and placebo users. [24]

In a Phase II trial of 55 HIV uninfected couples who used the gel or a placebo prior to each act of intercourse, no differences in side effects were reported in men exposed to the microbicide compared to those exposed to placebo. [25]

In vitro comparison of carrageenan and nonoxynol-9 (N-9) showed carrageenan to be 20- to 50-fold less toxic than N-9 to cervical and colorectal epithelial cells. [26]

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Drug and Food Interactions

Covalently coupled AZT and kappa-carrageenan are synergistic in vitro in tests of MT-4 cells incubated with HIV-1.[27]

Clinical Trials

For information on clinical trials that involve Carrageenan, visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: Carrageenan AND HIV Infections.

Dosing Information

Mode of Delivery: Intravaginal gel.[28]

Dosage Form: 3% gel inserted just prior to sexual activity and studied in applications up to once daily.[29] [30]

Prefilled, single dose, disposable, plastic Micralax® applicators providing delivery of approximately 4 mL gel.[31]

Chemistry

CAS Name: Carrageenan[32]

CAS Number: 9000-07-1[33]

Molecular formula: Unspecified[34]

Physical Description: Kappa carrageenan is a slightly opaque gel.[35]

Solubility: Kappa and lambda carrageenan are both soluble in very polar solvents. Kappa carrageenan is soluble in water above 60 C. Lambda carrageenan is soluble in water and in concentrated salt solution.[36]

Other Names

PC-515[37]

Carrageenin[38]

Carrageenan gum[39]

PC515[40]

Irish moss extract[41]

Further Reading

D'Cruz OJ, Uckun FM. Clinical development of microbicides for the prevention of HIV infection. *Curr Pharm Des.* 2004;10(3):315-36. Review. PMID: 14754390

Kilmarx PH, Supawitkul S, Yanpaisarn S, Jones H, van de Wijgert J, Young NL, Srivirojana N, Guest P. A year-long, randomized, controlled clinical trial of a carrageenan gel as a vaginal microbicide: Effect on reproductive tract infection (RTI) rates. *International AIDS Conf, Barcelona. Abstract WeOrD1318.* 2002.

Morar NS, Braunstein S, Jones H, Moodley M, Aboobaker J, Ndaba M, Ndlovu G, van de Wijgert J, Ramjee G. Safety of Carraguard® among HIV-positive women and men in South Africa. *Microbicides Conf, London. Abstract 02463.* 2004.

Perotti ME, Pirovano A, Phillips DM. Carrageenan formulation prevents macrophage trafficking from vagina: implications for microbicide development. *Biol Reprod.* 2003 Sep;69(3):933-9.

Manufacturer Information

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For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

References

1. Merck Index - 2001; p. 316
2. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 04/04/05.
3. Population Council - The Population Council's Lead Candidate Microbicide: Carraguard. Available at: <http://www.popcouncil.org/biomed/carraguard.html>. Accessed 04/04/05.
4. Merck Index - 2001; p. 316
5. Population Council - The Population Council's Lead Candidate Microbicide: Carraguard. Available at: <http://www.popcouncil.org/biomed/carraguard.html>. Accessed 04/04/05.
6. Intl AIDS Conf - 14th, 2002. Abstract WeOrD1318.
7. Intl AIDS Conf - 15th, 2004. Abstract ThOrB1374.
8. Merck Index - 2001; p. 316
9. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 04/04/05.
10. FMC Biopolymer - Available at: <http://www.fmcbiopolymer.com>. Accessed 04/04/05.
11. Merck Index - 2001; p. 316
12. Antimicrob Agents Chemother - 1988 Nov;32(11):1742-5
13. Population Council - The Population Council's Lead Candidate Microbicide: Carraguard. Available at: <http://www.popcouncil.org/biomed/carraguard.html>. Accessed 04/04/05.
14. Intl AIDS Conf - 14th, 2002. Abstract F11893.
15. Biol Reprod - 2003 Sep;69(3):933-9
16. Intl AIDS Conf - 14th, 2002. Abstract F11893.
17. Biol Reprod - 2003 Sep;69(3):933-9
18. Intl AIDS Conf - 14th, 2002. Abstract TuPeF5257.
19. Intl AIDS Conf - 14th, 2002. Abstract TuPeC4880.
20. Intl AIDS Conf - 14th, 2002. Abstract MoPeD3651.
21. Intl AIDS Conf - 14th, 2002. Abstract WeOrD1316.
22. Intl AIDS Conf - 14th, 2002. Abstract MoPeD3698.

23. Intl AIDS Conf - 14th, 2002. Abstract MoPeD3551.
24. Intl AIDS Conf - 14th, 2002. Abstract MoPeD3651.
25. Intl AIDS Conf - 15th, 2004. Abstract ThOrB1374.
26. Antimicrob Agents Chemother - 2004 Oct;48(10):3834-44
27. J Med Chem - 2002 Mar;45(6):1275-83
28. Population Council - The Population Council's Lead Candidate Microbicide: Carraguard. Available at: <http://www.popcouncil.org/biomed/carraguard.html>. Accessed 04/04/05.
29. Intl AIDS Conf - 14th, 2002. Abstract MoPeD3651.
30. Microbicides Conf - 1st, 2004. Abstract 02463.
31. Population Council - Population Council Microbicides Program--Carraguard® Clinical Testing. Available at: <http://www.popcouncil.org/biomed/candidate.html>. Accessed 04/04/05.
32. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 04/04/05.
33. USPD - 2003; p. 159
34. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 04/04/05.
35. FMC Biopolymer - Available at: <http://www.fmcbiopolymer.com>. Accessed 04/04/05.
36. Merck Index - 2001; p. 316
37. Biol Reprod - 2003 Sep;69:933-9
38. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 04/04/05.
39. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 04/04/05.
40. Medical Research Council of South Africa - Current Projects. Available at: <http://www.mrc.ac.za/hiv/projects6.htm>. Accessed 04/04/05.
41. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 04/04/05.